WS3.1 Gastric aspiration into the CF lung − relationship with reflux symptoms and lung function

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Objectives: Gastro-oesophageal reflux (GOR) is the retrograde movement of gastric contents up the oesophagus. This results in both classical and atypical symptoms. GOR is common in CF affecting 35–81% of patients and it may be associated with deteriorating lung function. We investigated microaspiration into the CF lung, characterised symptoms of reflux and compared these parameters with lung function.
Methods: FEV1 % predicted was recorded in 37 CF patients (19 male), mean age 29 (range 17–60) years. GOR symptom severity was assessed using the DeMeester Reflux score (0–9; <1 normal) and extra oesophageal reflux (EOR) using the Reflux Symptom Index (RSI) score (0–45; <13 normal). Pepsin (ELISA) and total bile acids (TBA) (mass spectrometry) were measured in the sputum of 29 and 24 CF patients respectively.
Results: Pepsin was identified in 17 of 29 (59%) (median 111 ng/ml) and TBA in 23 of 24 (96%) (median 0.18 μMol/L) patients. RSI scores showed atypical symptoms in 87% of patients, whereas, classical symptoms (DeMeester scores) were identified in 43% of patients. 88% pepsin-positive and 87% TBA-positive patients suffered EOR symptoms, however 53% pepsin-positive and 61% TBA-positive patients experienced GOR symptoms. FEV1 ranged from 12% to 101% of predicted (median 43%) but was not correlated with biomarkers or symptoms of reflux.
Conclusion: Gastric and biliary reflux into the lungs are very common in CF patients. EOR symptoms may be more closely associated with CF than GOR. Microaspiration of gastric content into the lung was not correlated with FEV1 and occurred across the spectrum of disease severity.

WS3.2 Higher levels of fecal calprotectin levels are associated with SIBO in cystic fibrosis after lung transplantation

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Objectives: Intestinal inflammation is a common complication of cystic fibrosis (CF). Small intestinal bacterial overgrowth (SIBO) has been discussed as prevalent determinant of intestinal inflammation in CF patients before lung transplantation (LuTx). Data on intestinal inflammation in post-transplant setting are scarce. Aim of this ongoing prospective study is to evaluate intestinal inflammation and its underlying mechanisms in CF patients after LuTx.
Methods: So far, 13 CF patients with LuTx (all with pancreatic insufficiency, median age 33 y, range 23–57 y; 43% male) attending our outpatient clinic were tested for intestinal inflammation by measuring of calprotectin in stool and IgG and IgA ASCA in serum. Intestinal infection was excluded by stool cultures, celiac disease by negative EMA/TTG antibodies. In 9 of 13 patients glucose-H2 breath test was performed to diagnose SIBO.
Results: Calprotectin was increased in all 13 patients (median 182 mg/kg, range 69–444 mg/kg). 12 of 13 (92%) patients were positive for either IgG (7 of 13, 54%) or IgA (9 of 13, 69%) ASCA. In 4 of 9 patients (44%) SIBO was diagnosed. Patients with SIBO had markedly increased fecal calprotectin levels (median 186 mg/kg, range 155–444 mg/kg) compared with patients without SIBO (median 135 mg/kg, range 69–146 mg/kg) ($p < 0.01$).
Conclusion: Intestinal inflammation was observed in all studied CF patients after LuTx as measured by increased fecal calprotectin and serum ASCA immunoglobulin levels. Patients with SIBO had noticeably increased fecal calprotectin levels, underlining SIBO as one of the crucial pathogenetic factors in intestinal inflammation in CF patients in post-transplant setting.

WS3.3 Molecular characterization of fecal microbiota and metabolic profiles association in cystic fibrosis patients

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Objectives: An early site of Cystic Fibrosis (CF) manifestation is the intestinal district. Clinical evidence indicates a role for intestinal microbiota in extra-pulmonary CF manifestations, along with impairment of patients' life quality. Gut microbiota seems to be involved in both human co-metabolism and toxicity/efficacy of drugs: a reported higher bacterial load in CF patients' gut could affect the quality of life. To describe through molecular techniques the fecal dominant microbiota and fecal/urinary metabolites in CF patients and controls.
Methods: Two patients' cohorts were engaged: 36 CF and 16 controls. Temporal Temperature Gel Electrophoresis (TTGE) was employed to have a 'snapshot' of predominant microbial community in fecal samples, and Solid Phase Micro Extraction-Gas Chromatography/Mass Spectrometry (SPME-GC/MS) was used to characterize fecal/urinary metabolites.
Conclusion: A separation between the two cohorts was found by means of TTGE ($\chi^2 = 6.107$, $P = 0.0135$) and fecal/urinary metabolites profiles ($\chi^2 = 11.827$, $P = 0.0006$). The multivariate analysis gave a model predictability of 95.5% for TTGE profiles, and 91.0% for SPME-GC/MS ones. We found a prevalence of *Escherichia coli* in CF and *Eubacterium limosum* in controls, reflecting an existing dysbiotic status in CF intestine. We also found peculiar toxic compounds such as cadaverine and putrescine in CF patients. Our results showed a predominant fecal microbiota associated with CF status, along with a peculiar CF fecal metabolite profile. These results could have a pitfall in diagnosis and CF patients' care.

WS3.4 *Clostridium difficile*, but not *Giardia lamblia*, is a frequent finding in the stool of CF-patients

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Objectives: *Giardia* and *Clostridium difficile* have been reported in up to 28%, respectively 50% of Cystic fibrosis (CF)-patients. Most of these patients remain asymptomatic, but villous atrophy with severe malabsorption (giardiasis) and severe, life-threatening *Clostridium difficile* enterocolitis has been rarely reported.
Methods: *Clostridium difficile* (C. diff.) and toxin A/B (C. diff. Check® [Alere, Köln, Germany]) and *Giardia lamblia* (Giardia II® [Alere, Köln, Germany]) were investigated in a single stool probe of 45 CF-patients >4 years of age (15.4±8.0 years old), 25 IBD-patients (21.2±1.8 years old) and 22 healthy relatives of CF-patients (controls) (21.4±13.2 years old). Exclusion criteria was an acute gastrointestinal or respiratory exacerbation 4 weeks prior to investigation.
Results: *Giardia* was detected in 9% of CF-patients and 0% of IBD-patients and controls (ns). *Giardia*-positive patients were significantly older than negative (25.4±10.8 versus 14.4±7.0; $p = 0.007$) and all were over 20 years of age (prevalence in this age group 28%). *Clostridium difficile* was detected in 76% of CF-patients, 20% of IBD-patients and 5% of controls ($p < 0.001$). *Clostridium difficile* toxin was found in 9% of CF-patients compared to 4% of IBD patients and 5% of controls (ns). All positive patients were asymptomatic. There was no significant difference with regard to BMI or antibiotic treatment.
Conclusion: *Giardia lamblia* is highly prevalent in CF-adults with 28%, but less frequent than reported. *Clostridium difficile*, but not toxin A/B, are regular findings (76%) independent of age and antibiotic therapy.